The Functional Organization of the Involuntary Nervous System and Its Humoral Mediators

By W. B. Cannon, M.D., *Boston, Massachusetts*

UNIVERSITY COLLEGE LONDON.
CANCELLED

54355.

The Functional Organization of the Involuntary Nervous System and Its Humoral Mediators*†

By W. B. Cannon, M.D., *Boston, Massachusetts*

We naturally think of ourselves as air inhabiting animals, but even a slight examination would show that we are separated from the air which surrounds us by a layer of dead cells in the outer horny portion of the skin or by a layer of mucus. All that is alive within these lifeless surfaces is bathed in a salty fluid—the *"milieu interne"*, as Claude Bernard called it, or the *fluid matrix*, as we may designate it. Thus our bodies have not only the external environment which other objects have but our living parts have also an internal environment composed of the rapidly flowing blood and the more slowly flowing lymph.

In relation to the external and internal environments we may separate the nervous system into two grand divisions. The division with which we are commonly acquainted, the so-called "voluntary system", attached to the bony skeleton, serves to change the external environment and our relations to it. This system also is supplied with surface sense organs, or exteroceptors, serving to acquaint us with our surroundings. Since our reactions to these surroundings are directed toward objects in the outer world, we may speak of this grand division of the nervous system as the *exterofective* system. The second grand division is the so-called "involuntary", "vegetative", or "autonomic" system which brings about changes in the internal environment. It may be regarded, therefore, as having *interofective* functions.

The Functional Characteristics of the Autonomic System

The functional characteristics of the interofective or autonomic division of the nervous system may be briefly summarized as follows.[1] Typically it innervates glands and the smooth muscles of the viscera, blood vessels, and skin. Whether it affects skeletal muscle is in question. Interposed between the smooth muscle or gland cell and the neurones reaching forth from the central nervous system there is invariably an outlying neuron, all of which is external to the central system. I have suggested[1] that this neuron may serve as an adapter or transformer of the nerve impulses so as to render them suitable for the visceral structures, which are more slowly act-

*Read before the American College of Physicians, San Francisco, California, April 8, 1932.

†From the Laboratories of Physiology, the Harvard Medical School.

22500893931

ing than skeletal muscle. The outlying neurones, whose cell bodies are commonly gathered in ganglia, are connected with the central nervous system by three sets of outreaching neurones, making three divisions—the cranial from the brain, the sacral from the sacral cord, and the sympathetic or thoracolumbar division from the spinal cord between the brachial and lumbar enlargements. The nerve fibers of these outreaching neurones, before coming to the outlying ganglia, are called *preganglionic*. Those passing from the ganglia to the viscera are called *postganglionic*. Commonly a single viscus is doubly innervated, by neurones from the middle or thoracolumbar division and from one of the terminal divisions. Thus the heart is supplied from the cranial division by the vagus nerves and also by fibers from the ganglia of the sympathetic. As a rule in this double innervation the representatives of the two divisions are opposed in action. For example, the vagus inhibits the heart beat and the sympathetic causes acceleration.

It is typical of the cranial and sacral divisions that their preganglionic fibers, reaching from the central nervous system to the outlying neurones, end in or near the viscera which they innervate. The fibers of the vagus nerves, for instance, pass directly into the heart muscle before meeting the relay. This arrangement is such as to provide for direct and particular action of these nerves without relation to one another. Thus the contraction of the pupil by way of the third cranial nerve, the flow of saliva by way of the seventh nerve, and the slowing of the heart by way of the tenth nerve are obviously separate and unrelated. The situation is quite different in the organization of the sympathetic or thoracolumbar division. In that division the preganglionic fibers reach out to a chain of ganglia, arranged on either side of the midline, from the superior cervical ganglion, near the corner of the jaw, through the chest and abdomen to the pelvis. These preganglionic fibers, after entering the nearest ganglion, pass through it and may reach downward or upward along the chain through two or three ganglia before coming to an end. This arrangement of the preganglionic fibers results in an overlapping of their distribution; in any ganglion there may be fibers from four or five different segments of the spinal cord. Or, to put it differently, fibers from any segment of the spinal cord may pass through four or five different ganglia of the sympathetic chain, giving off, in each one, collateral branches. This mode of organization has two effects. It greatly increases the area of distribution of the impulses coming out by any single fiber, and it also provides for diffuse distribution of impulses throughout the organism.

Confirmation of the idea that the sympathetic division is organized for diffuse distribution of effects is found in the facts that this division causes secretion of the substance adrenin into the blood, and that the circulating adrenin has practically everywhere in the body the same effects on the viscera as those produced by sympathetic impulses themselves. Obviously, even though the nerve fibers were not ar-

ranged for diffuse effects, the secreted adrenin would have such effects. The recent discovery of *sympathin,* which has, so far as we know, the same influence as adrenin, further emphasizes the view that the sympathetic division is organized for diffuse activity. In order to consider the rôle of sympathin it will be necessary to step back about twelve years and survey briefly the history of humoral transmission of autonomic nerve impulses.

The Humoral Transmission of Vagal and Sympathetic Impulses

In 1921 Loewi[2] reported the observation that Ringer solution, which has been in contact with a frog heart (A), while that heart has been under the influence of the vagal nerves, acquires a new property. When applied to frog heart (B), the Ringer solution as such has the same effect as the nerve impulses, i.e., it causes inhibition of (B). Loewi also found that when the frog heart (A) is subjected to sympathetic influence, the Ringer solution in contact with it when applied to heart (B) causes acceleration. Loewi's observations have been confirmed by others and have been reported as characteristic of other hearts than that of the frog. In 1930 Finkleman[3] published the interesting observation that when an excised piece of rabbit intestine (A), still supplied with its nerves, is placed so that Ringer solution which drops upon it will drip on another piece of excised rabbit intestine (B), the stimulation of the nerves of (A) causes inhibition of its spontaneous contractions and thereupon the spontaneous contractions of (B) are likewise inhibited. It appears that there is a substance given off from the intestine (A), when subjected to sympathetic impulses, that transfers to intestine (B) the effect of these impulses.

Further analysis of the substance produced when the vagus is stimulated has proved that it is dialyzable, that it is insensitive to acid but remarkably sensitive to alkali, and that, although quite stable while existing normally in undisturbed tissue, it becomes highly unstable when freed from such tissue by stimulation or when the tissue containing it is minced. These characteristics and also the mode of action of this "vagus substance" indicate that it is an ester of choline, and the conclusion has been drawn that it is probably acetyl choline.

The substance given off when the sympathetic supply to the heart is stimulated has many of the features of adrenin. Like adrenin it is destroyed when, after the addition of eosin, it is exposed to ultraviolet light; it is destroyed likewise by standing in air, and by being heated to boiling. It not only causes acceleration of the heart as adrenin does but also constriction of the arterioles.

The Belgian physiologist, Demoor,[4] has criticized the inference that these substances have any physiological significance, at least as circulating substances. He pointed out that the irrigation of isolated tissues with salt solution subjects these tissues to quite unnatural conditions and that under the circumstances cell permeability may be altered in such a way that ma-

terial may escape from the cells in a manner not at all physiological. So far as the "sympathetic substance" is concerned, that criticism can now be set aside, for it has been demonstrated that a material given off from smooth muscle when subjected to sympathetic influences may be carried in the blood stream to remote structures and there have typical effects.[12] In order to bring out this evidence we must consider the use of the denervated heart as an indicator.

The Denervated Heart as an Indicator of Increased Adrenin in the Blood

The heart may be wholly disconnected from the central nervous system by removing the upper thoracic sympathetic chains, by severing the right vagus nerve below the recurrent laryngeal branch (which is left to innervate the larynx), and by severing all of the cardiac branches of the left vagus trunk (which is left to control the gastrointestinal tract). Animals on which this operation is performed with careful surgical precautions live quite normally, and for many weeks there is no regrowth of nerve fibers to the heart.[5] The heart thus denervated is highly sensitive to circulating adrenin. It responds by a faster beat when adrenin is present in the almost incredible dilution of one part in 1,400,000,000 parts of blood.[6] By means of this sensitive signal of an increase in the concentration of adrenin in the blood stream it has been possible to show that adrenin is especially secreted when an animal is exposed to cold,[7] when it exhibits emotional excitement or exercises or moves about even slightly,[8] when it is subjected to asphyxia,[9] or is disturbed by hypoglycemia.[10] After momentary emotional excitement, for example, the heart rate may increase immediately 70 or even 100 beats a minute.

Now, if the adrenal influence is removed by extirpation of one adrenal gland and denervation of the other, the immediate increase of heart rate after excitement disappears. But after an emotional disturbance there is still seen a delayed cardiac acceleration which reaches a maximum in about three minutes. The explanation of this phenomenon was for a long time a mysterious and tantalizing problem. This delayed increase in the rate of the denervated heart continued after extirpation of the medulla from the remaining adrenal gland, after removal of accessory adrenal tissue in front of the aorta, after the destruction of the pituitary body, and after exclusion of thyroid, parathyroid, and gonadal influences. It seemed obvious that the effect must be due to some action of the sympathetic system because that was the system most prominently concerned with emotional expression. The phenomenon still continued, however, after both abdominal chains and all of the thoracic chains except a few ganglia in the lower thorax had been removed. The natural next step, therefore, was the removal of these remnants from the thorax. When that operation was performed the phenomenon disappeared. It seemed probable, therefore, that a substance was given off into the blood stream when the sympathetic was stimulated and this

substance was the cause of the delayed increase of the heart rate.[11]

The Presence of Sympathin and the Absence of "Vagus Substance" in the Circulating Blood

Experimental proof of the surmise which has just been expressed was obtained in an animal with the heart denervated, the adrenals excluded from participation, and the spinal cord transected in the midthoracic region. The hind part of the animal was thus isolated from the fore part (i.e., the brain), and could be experimented upon, therefore, without anesthesia. By this procedure it was found that stimulation of the sympathetic fibers governing the smooth muscles of the tail hairs would cause the typical belated acceleration of the heart and, associated therewith, an increase of blood pressure.[12] The same phenomenon occurred when the smooth muscles of the hairs of a patch of skin on the flank were stimulated. A check of the blood flow into and from the tail region, and also the removal of the patch of skin on the flank, caused the stimulation to become ineffective. Furthermore, it was found that the denervated salivary glands and denervated nictitating membrane could likewise be made to exhibit characteristic activities on exciting the smooth muscles of hairs in the hind part of the body.[13]

The substance that is thus discharged from stimulated smooth muscle resembles adrenin in acting on denervated structures just as the nerve impulses themselves act and, as has been recently learned, in being more effective after the injection of cocaine.[14] Since the substance does not come from the adrenal glands, however, but comes from other organs when subjected to sympathetic stimulation, it has been named "sympathin". Obviously, since sympathin is given off into the blood stream and since it acts like adrenin and coöperates with adrenin in mimicking sympathetic nerve impulses, its general distribution by the blood stream supports the view that the sympathetic division of the autonomic system is normally arranged for diffuse action over the widely spread sympathetic endings.

Success in demonstrating in the blood stream the presence of a sympathetic substance naturally raised the question whether it would not be possible to demonstrate by a similar method the presence of the vagus substance. In order to test this possibility we[15] used the denervated iris, submaxillary gland, and heart, as well as the denervated tongue and the normal blood pressure. We stimulated the entire distribution of the vagus nerve below the level of the heart. Furthermore, we arranged a by-pass for the portal blood so that it flowed into the inferior vena cava and thereby avoided the liver, which is destructive to acetyl choline.[16] Moreover, we used a variety of anesthetics and in some experiments excluded (by operations which rendered the animal incapable of experiencing pain) the necessity of using anesthesia. In spite of these very careful and thoroughgoing efforts, all our results were negative. We obtained no

general or remote effects as a consequence of vagus stimulation. It would appear, therefore, that the parasympathetic or vagal substance has a quite local influence. This conclusion, as will be noted, is in harmony with the view that the parasympathetic innervation serves for specific and narrowly localized action and not for diffuse effects.

It is of interest to observe that the organization of the autonomic system outlined above permits all sorts of variations, both general and individual. Thus, the heart, for example, may be made to beat less rapidly or more rapidly by varying the "tone" of the vagal influence up or down, without influencing other organs having a parasympathetic supply. Or, it may be made to beat less rapidly or more rapidly by varying the "tone" of the sympathetic supply; but in this case, because of the diffuse distribution of sympathetic influences, many other organs are involved in the reaction. I have elsewhere likened the condition to that of a piano. A note may be made louder by the vigor of the blow on a single key, or many keys may be influenced by pressing on the loud or soft pedal.

The General Services of the Autonomic System

At the outset the statement was made that the autonomic nervous system is interofective because it regulates conditions of the internal environment. Each of its three divisions has distinctive general functions. We obtain insight into those functions by considering the circumstances under which the several divisions are brought into action and also the effect which each produces. The sympathetic division is so specially concerned with preservation of constancy in the fluid matrix that we shall deal with it in detail. The other two divisions play an adjuvant rôle.

The functions of the *sacral division* may be summarized by the statement that they consist of a group of reflexes for emptying hollow organs which are periodically filled. Thus, sacral autonomic impulses cause contraction of the rectum and distal colon and also contraction of the urinary bladder. In both instances the effects are induced reflexly by a stretching of the tonically contracted viscera by their accumulating contents. Waste from organic activities is thereby eliminated. Distension of the seminal vesicles, though associated with more elaborate reactions, stimulates the *nervi erigentes* of the sacral division, and may thereby result in behavior which reflexly leads to a discharge of the accumulated fluid. To what degree the contractions of the distended uterus can be brought into this scheme is not quite clear. The fact that parturition can occur normally in the absence of the sympathetic division[17] indicates either that there is an intrinsic government of uterine contractions which is quite adequate, or that there are influences working by way of sacral fibers which have not yet been traced.

The functions of the *cranial division,* like those of the sacral, can be summarized as mainly a group of reflexes—reflexes protective, conserva-

tive, and up-building in their service. By narrowing the pupil of the eye the cranial division protects the retina from excessive light. By providing for the flow of saliva and gastric juice and by supplying the muscular tone necessary for the periodic contractions of the alimentary canal, it assures the essential basis for proper digestion and absorption of the energy-yielding material required for all bodily activity. By vagus control of insulin secretion it may play a rôle in the storage of glycogen in the liver. Further evidence of its conservative value is seen in the assurance of time for rest and recuperation of cardiac muscle by the tonic vagal slowing of the heart rate. The cranial division, like the sacral, has uncomplicated reflexes, such as the narrowing of the pupil, and likewise activities associated with affective states. The pleasurable taste and smell of food are accompanied by the so-called "psychic" secretion of the digestive juices, and by a tonic contraction of the stomach and intestines.

The two divisions—sacral and cranial—are similar in being largely subject to interference by striated muscle. Contraction of the bladder and rectum can be aided or frustrated by impulses from the cerebral cortex, much as the reactions of the pupil can be induced or modified by voluntary acts. Indeed, as a rule, the workings of the sacral and cranial divisions involve the coöperation of the cerebrospinal nervous system to a much greater degree than do the workings of the sympathetic division, because they are much concerned with external orifices surrounded by striated muscles.

The Rôle of the Sympathetic Division in Stabilizing the Internal Environment

In considering the services of the sympathetic division it is important to recognize the truth of the dictum laid down by Claude Bernard that just insofar as there is assurance of uniformity and stability of the internal environment, the organism is freed from the influence of changes in the external environment. The rôle of the sympathetic division of the autonomic system in governing the conditions of the internal environment can be clearly demonstrated in animals (cats, dogs, monkeys) which have had the sympathetic system entirely removed.[17] Let us consider some of the phenomena exhibited by such animals as compared with normal animals.

When a normal warm-blooded animal is exposed to cold surroundings there is an erection of hairs (if the animal is provided with that covering), a contraction of surface vessels which protects from heat loss, and a discharge of extra adrenin which accelerates metabolism and thus by production of extra heat serves to keep the temperature even.[7] Because of this arrangement for stable bodily temperature, warm-blooded animals are liberated from the limitations of inactivity that are imposed on cold-blooded animals during the winter season. Sympathectomized animals are clearly defective when exposed to cold. Pilomotor muscles are of course not under control and therefore the hairs are not erected. The smooth muscles of the blood vessels likewise are no longer

under nervous government. Cold has no local contractile effect on either of these structures. For these reasons there is no check on the heat loss from the body. Furthermore, the organism is unable to increase the secretion of adrenin and thereby to accelerate heat production when the body temperature tends to fall. The behavior of a sympathectomized animal in cold weather is in accord with this lack of physiological efficiency. During the winter it lives almost continuously in the neighborhood of sources of heat. If placed in a cold room having a temperature near freezing, the animal undergoes a rapid drop of the body temperature which brings about vigorous shivering. Shivering is the only resource, except exercise, that is left to protect sympathectomized animals from a seriously low temperature. It is noteworthy that what is lacking in such animals is the function of the sympathico-adrenal apparatus.

Not only does the sympathico-adrenal system protect against dangers from disturbing external conditions, it also protects against possible dangers from internal changes. Thus, as can be readily shown by giving insulin, the blood sugar may be reduced to a perilous degree. If it drops from approximately 100 mgms. per cent to 45 mgms. per cent, convulsions are likely to occur, and if the condition continues coma and death result. Ordinarily no such drop in blood sugar is permitted to occur. As soon as the concentration is reduced to a degree which approximates danger the sympathico-adrenal system is brought into action and sugar is liberated from the store in the liver.[10] The value of this arrangement can be easily demonstrated in animals from which the sympathetic has been removed or in which the adrenal glands have been rendered ineffective. Such animals have no means of increasing the blood sugar when it is reduced by insulin, and in consequence are extremely sensitive to action of that agent.[17]

Another internal situation from which dangers may arise is that of prolonged and vigorous physical struggle. Such struggle is accompanied by a great production of heat. The extra heat, which, if allowed to accumulate, would be disastrous, is eliminated by the pouring out of sweat on the body surface and the flow of blood through the surface vessels which have been cooled by evaporation of the sweat. Sympathetic activities are here always involved. Again, prolonged vigorous effort requires sugar as a source of energy. This is set free from the liver, —again by sympathico-adrenal influences. Furthermore, there is danger from the development of acid metabolites, especially lactic acid, arising from prolonged and vigorous muscular activity. This may result in markedly defective functioning of the neuromuscular system. It can be largely avoided by an abundant supply of oxygen which is used to burn the nonvolatile lactic acid into volatile carbonic acid. The volatile acid, unlike the nonvolatile, is easily discharged from the body. The extra oxygen is supplied to the tissues by a faster beating of the heart, by a faster blood flow owing to an increased blood pressure from splanchnic stimulation, and by the

availability of an additional number of circulating red blood corpuscles which has been set free from storage in the spleen. In all these adjustments the sympathetic or the sympathico-adrenal system plays an essential rôle. When animals are deprived of the service of this system, the adjustments are impossible. In consequence the ability of these animals to work is greatly reduced.[1]

Other illustrations might be given to show the ways in which the sympathetic division serves to keep uniform and stable the internal environment despite the potency of both external and internal disturbing conditions. Whenever the exterofective system goes into action and upsets the steady state which prevails in the fluid matrix while the organism is at rest, the interofective sympathetic system at once becomes an agent for restoration of the normal state. Unless it is overwhelmed it is quite efficient in maintaining the fitness of the internal environment for continued activity of the organism.[19]

The Disturbing Effects of Emotional Excitement

It is a matter of some moment that the bodily changes which occur in great emotional excitement are similar to those which occur in association with strenuous physical effort. The heart beats faster, the blood pressure rises, blood sugar is set free from the liver, there is a discharge of extra corpuscles from the spleen, and there may be sweating.[20] These striking alterations in the excited individual are best explained as preparation for action. That is, they are an exhibition of preparedness of the sympathetic division to protect the fluid matrix in case of struggle. Probably this association of sympathetic activity with excitement has developed in the course of myriads of generations of our ancestry. In wild life, where the struggle for existence is unmitigated, the emotion of fear is associated with the instinct to flee, and the aggressive feeling of rage is associated with the instinct to attack. If there is an attack, the organism attacked must either fight back or run. If there is flight, there is likely to be pursuit. In either situation the organisms involved may be engaged in a life-or-death struggle. Obviously the preparatory alterations of the body for such struggle would be useful.

For human beings who live in civilized society, the circumstances have been largely altered. There are occasions for great excitement and for the attendant bodily changes, but relatively few occasions for the struggle which naturally follows the excitement. Actual observations on students undergoing examination have shown that they are intensely wrought up and may have an increase of blood sugar to a degree that is seen in mild diabetes. In such conditions, also, digestion may be upset, the heart may beat at an unduly fast rate, and the other changes which we have been considering may be brought about. But there is no consequent action. The body prepares for a struggle when there is no struggle to be engaged in. The whole mechanism of reinforcing the body for great effort is set at work quite uselessly. The mechanisms which would keep

the internal environment fit now act in such a way as to be really disturbing. The result is that the complex group of emotional reactions which are valuable in more primitive conditions of existence may become a real menace.

The logical treatment of such a situation as has just been described may take two different directions. The situation may be regarded reasonably and the individual may say to himself, "There is nothing that I can do; consequently I will not get excited and stirred up. Being excited is proper when there is something that requires action, but that is not now." This suggestion of a rational attitude may seem an impossible counsel of perfection, but actually tests have shown that it can be made to work. If, however, it does not work and the agitation continues, the physiological mode of dealing with the situation is that of recognizing that the changes owing to excitement are directed towards efficient activity. The changes can best be met by going into action. Through sane and vigorous exercise the emotional disturbances have their natural consequences and the organism is not disturbed but is maintained in a stable state.

BIBLIOGRAPHY

[1]Cannon, W. B.: The autonomic system; Linacre lecture, Lancet, 1930, i, 1109-1115.

[2]Loewi, O.: Über humorale Übertragbarkeit der Herznervenwirkung, Arch. f. d. ges. Physiol., 1921, clxxxix, 239-242.

[3]Finkleman, B.: On the nature of inhibition in the intestine, Jr. Physiol., 1930, lxx, 145-157.

[4]Démoor, J.: Le réglage humoral dans le coeur, Ann. de physiol., 1929, v, 42-129.

[5]Cannon, W. B., Lewis, J. T., and Britton, S. W.: Studies on conditions of activity in endocrine glands. XVII. A lasting preparation of the denervated heart for detecting internal secretion, with evidence for accessory accelerator fibers from the thoracic sympathetic chain, Am. Jr. Physiol., 1926, lxxviii, 326-352.

[6]Anrep, G. V., and Daly, I. de B.: The output of adrenaline in cerebral anemia as studied by means of crossed circulation, Proc. Roy. Soc., London, 1925, xcvii, 450-463.

[7]Cannon, W. B., and others: Studies on conditions of activity in endocrine glands; the rôle of adrenal secretion in chemical control of body temperature, Am. Jr. Physiol., 1927, lxxix, 466-507.

[8]Cannon, W. B., and Britton, S. W.: Studies on conditions of activity in endocrine glands; the influence of motion and emotion on medulliadrenal secretion, Am. Jr. Physiol., 1927, lxxix, 433-465.

[9]Cannon, W. B., and Carrasco-Formiguera, R.: Studies on conditions of activity in endocrine glands. XI. Further evidence for reflex and asphyxial secretion of adrenin, Am. Jr. Physiol., 1922, lxi, 215-227.

[10]Cannon, W. B., McIver, M. A., and Bliss, S. W.: Studies on conditions of activity in endocrine glands. XIII. Sympathetic and adrenal mechanism for mobilizing sugar in hypoglycemia, Am. Jr. Physiol., 1924, lxix, 46-66.

[11]Newton, H. F., Zwemer, R. L., and Cannon, W. B.: Studies on conditions of activity in endocrine organs; mystery of emotional acceleration of the denervated heart after exclusion of known humoral accelerators, Am. Jr. Physiol., 1931, xcvi, 377-391.

[12]Cannon, W. B., and Bacq, Z. M.: Studies on conditions of activity in endocrine organs; hormone produced by sympathetic action on smooth muscle, Am. Jr. Physiol., 1931, xcvi, 392-412.

[13]Rosenblueth, A., and Cannon, W. B.:

Studies on conditions of activity in endocrine organs; some effects of sympathin on the nictitating membrane, Am. Jr. Physiol., 1932, xcix, 398-407.

[14]Rosenblueth, A., and Schlossberg, T.: Sensitization of vascular response to "sympathin" by cocaine and the quantitation of "sympathin" in terms of adrenalin, Am. Jr. Physiol., 1931, xcvii, 365-374.

[15]Freeman, N. E., Phillips, R. A., and Cannon, W. B.: An unsuccessful attempt to demonstrate humoral action of "vagus substance" in the circulating blood, Am. Jr. Physiol., 1931, xcviii, 435-440.

[16]Hunt, P.: Vasodilator reactions, Am. Jr. Physiol., 1918, xlv, 197; 231.

[17]Cannon, W. B., and others: Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses, Am. Jr. Physiol., 1929, lxxxix, 84-107.

[18]Dworkin, S.: The response of sympathectomized animals to insulin, Am. Jr. Physiol., 1931, xcviii, 467-474.

[19]Cannon, W. B.: The wisdom of the body, 1932, W. W. Norton, New York.

[20]Cannon, W. B.: Bodily changes in pain, hunger, fear and rage, 2 Ed., 1929, D. Appleton, New York.

WELLCOME INSTITUTE LIBRARY
Coll. welMOmec
Coll. pam
No. WL 600
1932
C22f